THE NEUTROPHILIC BLOOD PICTURE IN PERNICIOUS ANEMIA: A PRELIMINARY REPORT.

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In the course of some work on the Arneth blood picture in various conditions, the multiplicity of lobes of the neutrophiles in a case of pernicious anemia was observed. This particular point has since been studied in nine consecutive cases seen during the past year and in the stained smears from three others. The rather striking results found, together with the lack of mention of this feature in the text-books and monographs in general use, have prompted the publication of a preliminary report in order that further observations by others may be recorded.

So far as could be ascertained in a search of the literature, the only mention of similar findings were two. v. Decastello,[1] reporting a case of splenectomy for pernicious anemia, in speaking of the blood picture, noted the abnormal number of nuclei of the neutrophiles, "abnormen Kernpolymorphismus." Brosamlen,[2] in a discussion of the blood in pernicious anemia during remissions, stated that an Arneth shift to the right was present in all cases (seven), but gave no figures. All the standard text-books dismissed the neutrophiles in pernicious anemia with the statement that they were, as a rule, diminished, both relatively and absolutely.

In the present note attention is called to the fact that in ten out of twelve cases a decided increase in the normal number of lobes of the nuclei of the neutrophiles was found, *i. e.*, a "shift to the right" in the terms of Arneth. It is further shown for comparison that in eight cases of correspondingly severe anemia, not of the idiopathic pernicious variety, seven showed either a normal number, or a decrease in the number of lobes, a "shift to the left."

There is no intention of entering here into a discussion of the value of the Arneth count. In this work it has been utilized simply as a convenient method for the study and classification of the neutrophiles. As is well known, the neutrophiles can be divided into five classes according to the number of separate lobes of their nuclei. The classical formula of Arneth was 5 per cent. in the first class, 35 per cent. in the second, 41 per cent. in the third, 17 per cent. in the fourth, and 2 per cent. in the fifth. The majority of workers have reported formulæ approximating this, it being found remarkably constant in normal bloods. "Shifting to the left," or an increase in the lower classes at the expense of the higher, has been regularly found in most infections and in many other pathological conditions. "Shifting to the right," the opposite of this, although noticed occasionally, has not been considered characteristic of any particular condition.

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[1] Splenektomie bei perniziöser Anämie, Wien. med. Woch., 1913, xxvi, 951.

[2] Ueber die Bedeutung der Megalocyten bildund und über die Blutbefunde in den Remissionsstadien der perniziösen Anämie, Deutsch. Arch. f. klin. Med., 1913, cxii, 83.

In the present series the technique used in counting has been uniform and was given in detail in a former paper.[3] Differential counts were made on the basis of 500 leukocytes and nuclear counts on the basis of 200 neutrophiles. The five chief classes of the original Arneth were adhered to with the "index" as the sum of the first, second, and one-half the third classes, a figure arbitrarily adopted as an easy means of comparison. Nuclei connected by anything more than the finest thread were counted as single. Nuclei plainly superimposed upon another were classed separately, and where doubt existed the cell was not tabulated.

The cases were from the medical service of the University of California Hospital and the private practice of Doctor Herbert C. Moffitt. Patients' histories are not given, but of the cases in Table I the diagnosis was made in each of idiopathic pernicious anemia of Biermer, both from a clinical and a hematological standpoint. In Table II the clinical diagnosis is given. For the sake of brevity descriptions of the red cells are omitted. In all the pernicious anemia cases, however, they exhibited the characteristic changes to greater or less degree, *i. e.*, increase in average diameter, high color, alterations in shape and size, and abnormal variations in staining reaction. In the other cases the diameter was normal or less than normal, central pallor was marked, and the various other pathological changes were less noticeable.

Discussing briefly the findings shown in Table I, it will be noted that Cases 1, 3, 5, 6, 7, 9, 10, 11, and 12 present distinctly abnormal neutrophilic pictures, in that at least three-fourths of the cells have three or more pieces to the nucleus. It may be remarked parenthetically that class five contains those cells having five or more lobes. and not infrequently nuclei may be seen having as many as eight separate pieces. Cases 2 and 8 show normal formulæ. The first observation on Case 4 shows a shifting to the right, but the two subsequent examinations show counts which come just within the normal range. The severity of the case has apparently no bearing on the degree of shifting, Cases 4 (at the time of the first observation), 6, and 9 being the gravest of the series. Case 7 was in excellent condition, yet showed a tremendous alteration in his picture. Seemingly against this statement is the fact that in Cases 4 and 10, as the general condition improved, the neutrophiles approached the normal, and in Cases 5, 6, and 9, as the

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[3] Le Roy H. Briggs, The Clinical Value of the Arneth Method of Blood Examination, California State Jour. Med., 1912, x, 337.

TABLE I.—PERNICIOUS ANEMIA.

Case number.	Date.	Hemoglobin. (Dare) per cent.	Red blood cells.	Normoblasts, per c.mm.	Leukocytes.	Neutrophiles, per cent.	Large mononuclears and transitionals, per cent.	Lymphocytes, per cent.	Eosinophiles, per cent.	Basophiles, per cent.	Myelocytes, per cent.	Neutrophiles.					
												Class I.	Class II.	Class III.	Class IV.	Class V.	Index.
Case 1, J. R. S.	April 1, 1909	38	1,609,000	Few	2,800	62.8	2.8	31.2	3.2	0	0	0	20.0	35.0	34.0	11.0	37.5
Case 2 U. C. H., No. 2752	Sept. 26, 1910	40	2,292,000	Few	4,800	71.4	4.0	21.6	3.0	0	0	2.5	27.0	43.5	22.5	5.0	51.25
Case 3, Li.	Sept. 11, 1912	45	1,968,000	0	6,000	74.0	3.8	20.6	1.2	0.4	0	2.5	16.0	42.0	28.5	11.0	39.5
Case 4 U. C. H., No. 5298	Feb. 18, 1913	10	510,000	700	2,100	56.6	6.6	36.6	0.2	0	0	2.0	13.0	40.5	34.5	10.0	35.25
	April 8, 1913	45	2,372,000	0	5,000	50.0	8.0	37.4	4.6	0	0	3.5	25.0	45.5	18.0	8.0	51.25
	Oct. 15, 1913	55	2,872,000	0	7,500	51.6	12.0	30.4	5.6	0.2	0	5.5	25.0	39.0	25.5	5.0	50.0
Case 5 U. C. H., No. 5550	April 15, 1913	45	2,228,000	0	4,000	65.6	5.6	26.8	1.6	0.4	0	0	16.0	49.5	28.0	6.5	40.75
	May 5, 1913	50	2,996,000	0	4,200	57.2	8.4	30.0	4.0	0.4	0	0.5	22.5	51.0	21.0	5.0	48.5
	Dec. 20, 1913	40	2,406,000	Few	5,400	53.4	12.8	27.8	5.8	0.2	0	0	9.5	47.0	29.5	14.0	33.0
	Jan. 7, 1914	35	2,841,000	0	7,100	66.6	9.4	22.0	1.8	0.2	0	0	13.0	42.5	34.0	10.5	34.25
Case 6 U. C. H., No. 5582	April 28, 1913	15	1,078,000	400	2,800	59.0	7.0	31.6	2.4	0	0	3.0	17.5	39.5	29.0	11.0	40.25
	May 5, 1913	20	969,000	1600	4,800	73.8	2.4	21.0	2.2	0.4	0.2	2.0	10.5	42.5	26.0	19.0	33.75
Case 7, Ha.	May 26, 1913	60	2,504,000	0	9,300	64.4	4.4	26.2	5.0	0	0	0	4.5	24.0	38.5	33.0	16.5
Case 8 U. C. H., No. 6279	Oct. 8, 1913	55	2,960,000	Few	8,100	61.0	12.2	24.0	2.6	0.2	0	3.5	36.5	44.0	15.0	1.0	62.0
	Dec. 9, 1913	70	4,920,000	0	5,900	53.4	10.4	31.0	4.2	1.0	0	4.0	30.0	50.0	14.5	1.5	59.0
	Feb. 27, 1913	80	5,672,000	0	7,200	48.6	11.0	38.8	0.8	0.8	0	1.0	22.0	49.0	22.5	4.0	48.25
Case 9, Hf.	Dec. 4, 1913	25	955,000	500	5,100	62.6	2.6	33.0	0	0.2	1.6	6.0	17.5	35.0	25.0	16.5	41.0
	Dec. 12, 1913	20	736,000	400	7,000	72.0	1.4	25.6	0	0.2	0.8	2.0	11.0	30.5	31.0	25.5	28.25
Case 10 U. C. H., No. 6598	Dec. 19, 1913	35	2,172,000	Rare	5,100	80.6	5.8	13.4	0.2	0	0	0.5	15.0	29.0	32.0	23.5	30.0
	Jan. 16, 1914	55	3.100.00	0	6,600	57.2	11.8	28.2	1.8	1.0	0	1.0	17.5	41.5	27.0	13.0	39.25
	Feb. 10, 1914	60	3,904,000	0	5,100	48.2	7.6	39.4	3.6	1.2	0	1.0	20.5	45.5	26.5	6.5	44.25
Case 11, Gn.	Jan. 3, 1914	40	1,500,000	Few	5,000	65.4	4.0	26.4	3.6	0.2	0.4	1.5	10.5	28.5	34.0	25.5	26.25
Case 12, Hu.	Feb. 27, 1914	50	2,146,000	Few	7,200	61.2	3.8	33.6	1.0	0.2	0.2	1.5	16.0	38.5	31.5	12.5	36.75

TABLE II.—SECONDARY ANEMIA.

Case number.	Diagnosis.	Date.	Hemoglobin. (Dare) per cent.	Red blood cells.	Normoblasts per c.mm.	Leukocytes.	Neutrophiles, per cent.	Large mononuclears and transitionals per cent.	Lymphocytes, per cent.	Eosinophiles, per cent.	Basophiles, per cent.	Myelocytes, per cent.	Neutrophiles.					
													Class I.	Class II.	Class III.	Class IV.	Class V.	Index.
Case 1 Pa.	Sarcoma of tongue.	Jan. 16, 1913	35	2,260,000	0	8,300	67.0	8.8	24.0	0	0.2	0	13.0	54.0	32.5	0.5	0	83.25
Case 2 U. C. H., No. 5309	Nephritis, syphilis, terminal pericarditis.	Feb. 20, 1913 Feb. 25, 1913	15	1,800,000	0 Few	14,400	79.6 84.6	3.6 7.4	10.8 6.2	4.6 1.4	1.4 0.4	0 0	3.5 8.5	37.0 45.0	43.0 40.0	15.0 6.5	1.5 0	62.0 73.5
Case 3 U. C. H., No. 5838	Possible Banti.	June 28, 1913 Sept. 24, 1913	50 60	3,120,000 3,720,000	0 0	5,100 6,200	65.8 58.8	8.8 7.0	18.4 16.4	6.6 16.4	0.4 1.4	0 0	18.0 16.0	57.5 59.0	22.5 24.5	2.0 0.5	0 0	87.25 87.25
Case 4 U. C. H., No. 5848	Syphilis	June 28, 1913	38	3,000,000	Rare	9,700	65.4	6.2	28.4	0	0	0	2.5	13.0	47.0	26.5	11.0	39.0
Case 5 U. C. H., No. 5828	Duodenal ulcer with hemorrhage	June 28, 1913	20	2,064,000	0	9,900	69.0	15.0	15.8	0	0.2	0	7.0	38.0	40.5	11.5	3.0	65.25
Case 6 U. C. H., No. 5944	Cirrhosis of liver with hemorrhages	July 20, 1913	18	1,516,000	Rare	14,400	73.6	4.2	21.8	0.4	0	0	2.5	35.0	41.0	18.5	3.5	58.0
Case 7 U. C. H., No. 6379	Chronic lymphatic leukemia	Oct. 24, 1913	35	2,550,000	Many	225,000	2.0	1.0	97.0	0	0	0	19.5	43.5	25.5	7.5	4.0	75.75
Case 8 U. C. H., No. 6485	Probable malignancy of intestine.	Nov. 17, 1913 Dec. 10, 1913 Jan. 15, 1914	10 10 18	1,800,000 2,400,000 2,312,000	0 0 250	11,900 11,800 14,200	64.2 72.0 75.8	14.3 9.2 10.8	17.9 13.4 10.8	2.7 4.4 2.2	0.4 1.0 0.4	0.3 0 0	4.5 3.0 2.5	40.5 31.0 36.5	43.0 52.5 43.5	10.5 10.5 16.0	1.0 3.0 1.5	66.5 60.25 60.75

general condition grew worse, the shifting to the right became more marked. Case 8, an early case which improved greatly, however, presented normal formulæ at two observations and a very slight shifting to the right at a third.

Table II is inserted simply for comparison as showing eight consecutive cases of approximately similar grades of anemia, not, however, of the idiopathic type. Only one of these, Case 4, shows a shifting to the right. The anemia in this case was beyond question a secondary one, but further observations were unfortunately not made. Cases 5 and 6, both anemias of rapid onset, showed normal neutrophilic pictures. Case 2 at the first examination and Case 8 throughout also showed normal formulæ, although the former died the day following the second count, and the latter was in very bad condition. The others showed a moderate degree of shifting to the left, a not unexpected finding.

Nothing further can be said in this note. Its purpose is simply to call attention to the increased number of nuclear particles of the neutrophiles in pernicious anemia, a point doubtless noticed many times before, but evidently worthy of further study.